Screening and Diagnosis of Dementia in People with Down's Syndrome: Implications of using the DLD Questionnaire

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Title

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Abstract

Objective: The Dementia Questionnaire for People with Learning Disabilities (DLD) is one of the main screening and monitoring tools for dementia in people with Down's syndrome (DS). As part of a quality improvement project to improve care for people with DS and dementia in an intellectual disability (ID) service, we studied the screening and monitoring process by retrospectively investigating the use of DLD and exploring clinicians' experience of using it.

Method: DLDs completed in the service was retrospectively assessed. Changes in DLD scores were matched against people who received a clinical diagnosis of dementia. Data was analysed to estimate sensitivity, specificity and predictive values of DLD. A questionnaire was used to assess clinicians' experience.

Results: Data for 20 service users was collected. DLD cognitive scores showed 80% sensitivity and 60% specificity for the diagnosis of dementia, with a positive predictive value of 40% and negative predictive value of 90%. Staff found DLD to be easy to perform but time-consuming. This led to preparation of a decision tool for appropriateness of performing a DLD.

Discussion: Our results show that a negative DLD helps to exclude dementia where there is concern over cognitive decline, but a positive result is not specific enough to suggest the possibility of dementia. This shows that DLD may have limitations if used as a screening tool alone but could be used for the monitoring of the disease trajectory of those with a confirmed diagnosis as well as to establish a baseline DLD when a person is screened for dementia first.

Background

Dementia is a neurodegenerative disorder with a progressive decline in memory and other cognitive functions. It is more prevalent in people with Down's Syndrome (DS) compared to the general population (1). People with DS represent the largest group of dementia sufferers under the age of 50 years (2). Studies have reported prevalence to range from 4-55% in 50-59 year_–olds (2). Difficulties in estimating prevalence ultimately stems from diagnostic uncertainty, as the diagnosis of dementia is rooted in clinical history of decline in cognition. It is further challenged due to a prolonged pre-clinical phase presenting with nonspecific symptoms that do not meet the criteria for dementia. People with DS can present with executive function deficits along with behavioural and psychological symptoms before developing memory deficits (3). Assessment of cognitive functions can beis challenging in people with DS compared to general population as people with DS may already have reduced intellectual and executive functioning at baseline presentation, causing a floor effect on standardised tests. Intra-individual fluctuations in performances during standardised tests add another layer of complexity (4). Presence of mental illnesses such as depression, delirium, other physical and mental comorbidities and sensory abnormalities further complicates the presentation (5). Hence the clinical assessment of dementia in ID requires skilful establishment of a decline in cognitive functioning from current level.

Despite these challenges, identifying individuals with DS and dementia is important. Early diagnosis can influence morbidity and mortality in people with ID. Sinai et al 2017 in their study showed athe reduced life expectancy of people with DS with a median survival time of 3.7 years after the diagnosis to death (6). Eady et al 2018 in their naturalistic longitudinal follow up study showed that people with DS and dementia on anti-dementia medications had a significantly higher median survival time compared to those who were not on medications (7). Diagnosing dementia early also helps families and carers to understand changes the person with DS goes through and plan future care (8).

Therefore, improving strategies to detect dementia in people with DS is important. There are several tools used for screening and diagnosis of dementia in people with DS. These tools aim to detect functional decline over time indicating the worsening of dementia. Working groups looking in to the diagnostic process of dementia in ID have suggested initial assessment of premorbid functioning followed by annual reassessments using battery of tests (9). However,

~~authors of this study highlighted the~~there are challenges when using a battery of tests; for example, differentiating change associated with ageing from that associated with dementia can be challenging. It has been stipulated that~~and stipulated~~ the use of different tests and strategies could~~to~~ minimise any pitfalls, even though~~.~~ the risk of~~There are many~~ biases (such as ~~including~~ interviewer bias, recall bias and response bias) remains when using these tests (9) ~~when administering these batteries of tests~~.

One of the tests widely used in intellectual disability mental health services is the Dementia Questionnaire for People with Learning Disabilities (DLD) formerly known as the DMR (10). The DLD was developed in the 1980s in Netherlands, and its intended use was for adult with ID including those with a diagnosis of DS. Since then, it has been used widely in Europe and in the UK, both in clinical practice as well as in research (11). It is completed by a family member or carer that knows the person well. It has 50 items giving two main scores, namely cognitive scores (SCS) and social scores (SSC). There are eight sub-scales (short-term memory, long-term memory, spatial and temporal orientation, speech, practical skills, mood, activity and interest and behavioural disturbance). Even though Evenhuis (1992) reported that the DMR has a sensitivity of 100% (10), other studies have shown that DLD has lower sensitivity and specificity (0.61/0.63) despite its wide usage (12,13). Studies have shown how individual carers' perceptions of decline in function can influence the outcome of the DLD assessment. Interrogating a pair of informants about the same person with ID using DLD scores results in "good" agreement in only 15% of cases, and almost 20% of informant pairs disagree significantly (14). Additionally, the DLD score is significantly influenced by the degree of ID prior to the assessed functional decline.

Despite these challenges, DLD is routinely used ~~in a specialist clinic~~ to assess for ~~mental health and~~ cognitive declines in~~for~~ people with Down's Syndrome in an urban specialist clinic in London. As part of a quality improvement project to assess the diagnostic pathway for dementia for people with DS, a study was carried out to assess the use of DLD and user experience and what can be done to improve this pathway.

Aims

To assess experience of DLD in the clinic and improve its future use in the service, we designed this study aiming to:

1) Investigate and understand the current attitudes and experiences of staff using DLD.
2) Investigate the performance of DLD in identifying dementia in our patient population, when compared to diagnosis through comprehensive clinical assessment.
3) Prepare a decision tool to identify situations where the use of DLD could be beneficial.

Methods

Assessing staff experiences

We prepared a staff questionnaire using a mixed qualitative-quantitative formulation. We asked three questions:

(1): "How confident are you in your ability to work through a DLD questionnaire with a carer of a person with an intellectual disability?"

(2) "How helpful do you find the DLD questionnaire to be in considering dementia in a person with intellectual disability?"

(3) "How helpful do you find the DLD questionnaire to be for monitoring progression of dementia in a person with intellectual disability?".

Answers were given on a rating scale of one to four, where "1" was "not at all", "2" was "very little", "3" was "somewhat" and "4" was "very". Free-text fields were also included with each question to allow additional comment. The questionnaire was prepared using the Microsoft Forms tool and disseminated to all staff members who routinely perform DLD as a part of their practice.

Assessing DLD performance as a diagnosis and screening tool

We designed a clinical research form in order to collect data on all patients open to the DS Clinic. We collected data on a) age, b) the presence of a formal diagnosis of dementia, c) the date of dementia diagnosis, and d) data on DLD outcomes for all DLDs completed for all service

users. Data collected on DLD outcomes included a) the date of DLD assessment (or assessments), b) the sum of cognitive scores (SCS), and c) the sum of social scores (SOS). DLDs were completed by a variety of health professionals, including physicians, mental health nurses, intellectual disability nurses, occupational therapists, psychologists, and physiotherapists. This reflects the real-life use of DLD questionnaire in ID community services. Service users with a single DLD score were excluded as a minimum of two scores were needed to compare results longitudinally.

Data collected using the DLD was then used to calculate sensitivity, specificity and the false positive rate of DLD for a diagnosis of dementia in this population. ~~The diagnostic cut-off points were: A~~a single increase of 7 or more points in SCS and/or a single increase of 5 or more points in SOS were regarded as indicative of dementia in this study ~~, throughout the patient record~~as recommended when using DLD. For individuals with more than two DLD assessments on record, we treated any single sufficient increase as a positive DLD test result.

We organised the outlined data in two-by-two tables and calculated sensitivity, specificity, false positive rate, and negative predictive value. We reported those values to the nearest whole percentage point.

Preparing a clinical decision tool

The data obtained in the staff questionnaire, data regarding performance of DLD as a diagnostic and screening tool, and other evidence from previous studies, were used to prepare a clinical decision tool to inform staff decisions on performing DLD when seeing DS service users in our clinic.

Results

Aim 1: to assess performance of DLD as a diagnostic and screening tool

Our clinic accepted a total of 67 adults with DS since its inception. We identified a total of 20 service users who had at least two DLD assessments performed and documented in the electronic health record (figure 1). Of those 20, 10 service users had 3 or more DLD

assessments completed. A total of 60 individual DLD assessments were performed. Assessments were performed either as a screening in patients above 40 years of age in DS clinic, or due to a concern over functional decline. Clinical diagnosis of dementia was made by consultant psychiatrists following a details psychiatric assessment. This was used as the gold standard test (15) to confirm the diagnosis.

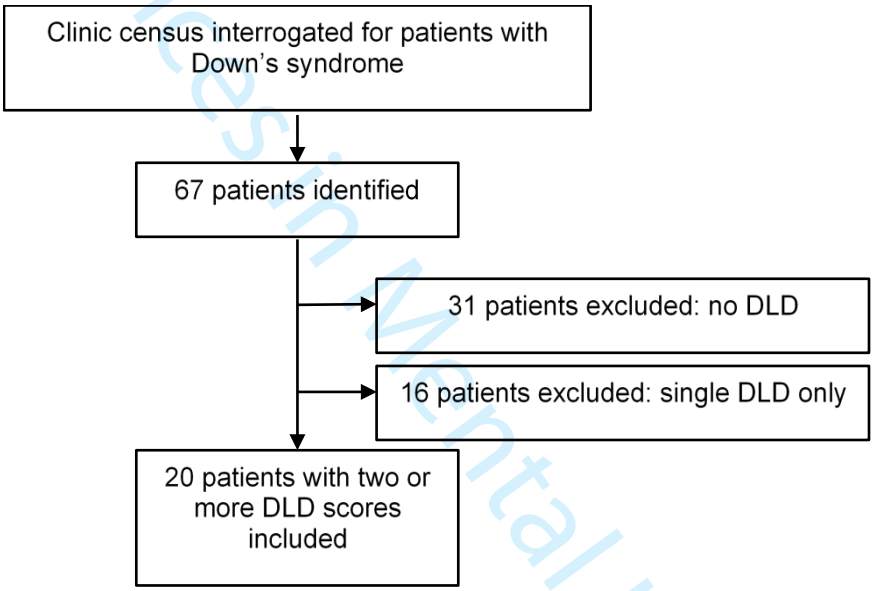


Figure 1. Flow-chart outlining patient recruitment process

This sample consisted of 12 female and 8 male participants. Mean age was 55 years (range 44-70). A total of 5 people (25%) received a diagnosis of dementia following a psychiatric assessment. The assessment included a structured history and examination of the person with DS and a collateral history whilst excluding other causes of cognitive decline. The average age at diagnosis of dementia was 53 years old.

Table 1: Sensitivity and specificity two-by-two tables for DLD Cognitive scores in diagnosis of dementia. N=20.

	SCS increase of ≥ 7 points between assessments	No SCS increase of ≥ 7 points between assessments
Confirmed diagnosis of dementia (5)	4	1

No diagnosis of dementia (15)	6	9

Table 2: Sensitivity and specificity two-by-two tables for DLD Social scores in diagnosis of dementia. N=20.

	SOS increase of ≥ 5 points between assessments	No SOS increase of ≥ 5 points between assessments
Confirmed diagnosis of dementia (5)	1	4
No diagnosis of dementia (15)	4	11

Longitudinal increase in DLD SCS was 80% sensitive (Table 1): 4 out of 5 service users diagnosed with dementia had a concurrent significant increase in cognitive scores. Social scores proved less sensitive in this small sample: only 1 of the 5 patients with dementia had an increase in SOS of 5 or more.

DLD proved to be less specific at those cut-off scores (Table 2): DLD SCS was 60% specific and DLD SOS was 73% specific in excluding the diagnosis of dementia. The false positive rate was thus 40% and 27% for cognitive and social scores, respectively. The negative predictive value of increase in DLD SCS was 90% and the positive predictive value for DLD SCS was 40%.

There were s~~S~~ervice users who had a significant DLD score increase but were not diagnosed with dementia following clinical assessment. Some of these service users had ~~also had~~ a change in baseline scores following a change in circumstances, e.g. moving between the care facilities, or due to a change in their usual carer. Those DLD scores improved on subsequent DLDs. In other~~some~~ cases, the reason for apparent decline in function was multifactorial and included both physical and mental health problems. In the majority of cases, the repeat DLDs were performed by different healthcare professionals and, in some cases, with different carers. The inter-informant reliability of DLD is only 15% and so this may have contributed to variance of baseline over time.

Aim 2: To understand staff experience

A total of eight~~8~~ members of staff completed the questionnaire: three~~3~~ members of the nursing team, one~~1~~ occupational therapist, two~~2~~ social workers and two~~2~~ doctors.

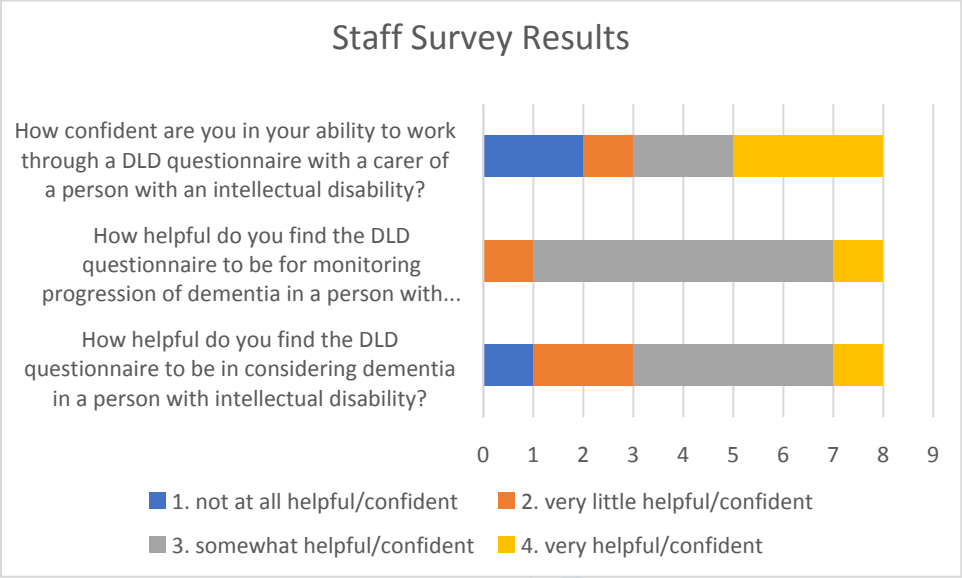


Figure 2. Results from staff survey (n=8) asking the following 3 questions: 1. How confident are you in your ability to work through a DLD questionnaire with a carer of a person with an intellectual disability? 2. How helpful do you find the DLD questionnaire to be for monitoring progression of dementia in a person with intellectual disability? 3. How helpful do you find the DLD questionnaire to be in considering dementia in a person with intellectual disability?

The level of confidence in working through the DLD with a carer varied (Figure 2). Five~~5~~ out of eight~~8~~ (63%) staff members rated their confidence level at "somewhat confident" or "very confident". Staff who felt confident with delivering the DLD explained their answer with (a) being familiar with the form structure, (b) having undertaken many DLDs in the past, and (c) the form being simple and self-explanatory. Staff who did not feel confident attributed this to (a) low exposure to the use of DLD and (b) training needs/lack of training.

Five~~5~~ out of eight~~8~~ (63%) staff members considered the DLD to be "somewhat helpful" or "very helpful" in considering dementia in a person with ID. Some members of staff pointed out that the DLD is "very subjective" i.e. carer-dependent. Two~~2~~ (25%) staff members identified the need to review the effectiveness of DLD. A staff member also pointed out that the result may be confounded by the level of ID or a co-existing mental health diagnosis.

The m~~M~~ajority of staff agreed that the DLD is somewhat helpful in monitoring the progression of dementia once it is diagnosed. A member of staff pointed out that the DLD can be completed annually to monitor change in a patient with ID and dementia. Three~~3~~ other participants remarked on the usefulness of DLD in monitoring for change in dementia being affected by inter-rater discrepancy "the difference in DLD scores obtained from different carers".

50% of staff members declared that the time spent on completing the DLD is typically over 20 minutes.

In summary, concerns about using DLD included the length of time to complete the form, inter-respondent variability, poor phrasing and repetition of questions, and ambiguity over indications for its use. Members of staff also noted that they were uncertain of when to perform DLD when seeing a service user with DS. However, staff found DLD useful in some ways, citing ease of use and minimal training requirements. Importantly, staff identified that DLD is widely used across many intellectual disability services, allowing standardised comparison of functional abilities against a baseline that may have been obtained elsewhere.

Discussion

DLD is commonly used for screening, monitoring and diagnosis of dementia in people with DS in intellectual disability and mental health services in the UK. This quality improvement project attempted to understand the use of DLD in day-to-day clinical practice and to suggest improvements to pathways for screening and monitoring of dementia in people with DS.

DLD in this clinic setting was used for two different purposes. Firstly, it was used as a screening tool to identify people with DS and dementia at an early stage. Secondly, it was used as a tool to monitor when a person with DS is diagnosed with dementia. Recognising people with DS at a very early stage of dementia is often clinically challenging due to the nature of non-specific symptoms (16). This is more challenging specially during the prodromal stage of dementia when symptoms are not severe enough to meet the diagnostic threshold. This makes it challenging to develop screening tools to detect early stages, particularly prodromal phases of dementia.

Our study showed a negative predictive value of 90% for a stable SCS in DLD. This suggests that DLD without a change in repeated scores is useful for excluding a diagnosis of dementia in the context of suspected dementia. Our results also showed that an increase in DLD scores is~~to be~~ less useful in confirming dementia in people with DS, given the positive predictive value of 40% for the DLD SCS scores. Interpretation of these findings to apply in clinical practice can be challenging as validity of scores are influenced by multiple factors including confidence of the carer giving information to complete DLD. Reliability of DLD is affected by poor inter-rater reliability, as identified in our staff experience and other studies. One can argue if this can be replaced by few generic questions to establish if there has been any change in functioning of an individual. If there is no evidence for any change, there may not be a need to carry out a DLD. However, if there is doubt, a DLD may be useful as a stable DLD score will suggest that it is unlikely to be due to dementia. If there is a positive DLD, this will suggest the need for a psychiatric assessment for dementia.

Our results showed that sensitivity was 80% for DLD SCS and 20% for DLD SOS. Specificity was 60% for DLD SCS and 73% for DLD SOS. The results are comparable to those of Rosner et al. (2021), who used the same cut-off scores in 71 patients, and found that the sensitivity values ranged from 58.3% to 72.2%, and the specificity values from 62.9% to 71.4% (12). Previous literature reports the sensitivity and specificity separately for both SCS and SOS scores to have varied considerably (13,17). It has been suggested that when the criteria are modified to include a combination of the two scores, the specificity improves, and sensitivity remains acceptable (18).

From an epidemiological perspective, a screening test must be both reliable (consistent) and valid (sensitive and specific). Our data estimates the false positive rate are 40% and 27% for cognitive and social scores, respectively. Administering a DLD to every service user annually would therefore likely lead to over-investigation and over-referral to dementia clinics.

Factors that may affect the sensitivity and specificity include the fact that DLD may fail to identify vascular dementia; moreover, organic illness, depression and sensory disability may lead to false positive results (17). Behavioural problems in the absence of dementia have also been reported to contribute to false positive results (18).

Strengths of our study include the fact that we have established the validity of the DLD in a particular service, by comparing outcomes with clinical diagnosis of dementia; our study therefore helpfully adds to the literature on the validity of the DLD for use in patients with Down Syndrome and intellectual disability. Moreover, we have also obtained quantitative and qualitative information on clinicians' experience with using the DLD, which is also new and useful information on the practical acceptability of the instrument. Limitations of our study include the fact that the final sample size is fairly small (20 patients) and therefore results obtained may not be accurately representative in this case. Furthermore, given the small sample size we were unable to make any recommendations about altering the commonly-used cut-off scores.

Considering all the above, we have prepared a decision-making tool (Appendix 1) to be used to decide if DLD should be performed when seeing a person with DS. The tool is designed to advise if performing a DLD is necessary for the patient. The first step involves whether there is concern over a decline in function. Early signs of Alzheimer's disease in Down's syndrome may often include a decline in executive functioning (19). For example, the person may need to be prompted, may stop mid-task and wander off, may not be able to follow the steps of a task, and not realise when making errors (20). There may be a change in various daily activities, including personal care, showering, dressing, preparing a simple meal or a hot drink.

In cases where there are concerns about function declining, we suggest that a DLD should be recorded. When there is an SCS increase ≥ 7 and/or an SOS increase ≥ 5 we suggest that a referral for a psychiatric assessment should be made. At this point, there should be consideration of requesting a full health screen and relevant bloods by the GP (21). This would allow to rule-out reversible causes of dementia and delirium, including hypothyroidism, infection, and folic acid abnormalities (e.g. in patients taking anticonvulsants) (22). A mental state examination should also be performed, and a diagnosis of depression rather than cognitive decline should be considered in cases where symptoms appear to fluctuate (22). Where indicated, the clinician may consider requesting a CT or MRI brain scan to further investigate the decline in function (21).

When there are no reported concerns about a decline in function, a DLD should still be recorded in cases when there is no previous baseline DLD. This would allow longitudinal

follow-up of any decline in function in the future. We suggest annual contact to determine whether there have been any concerns about changes in function, and if this is the case to follow the steps described above. We also suggest that annual contact should be made in cases where a psychiatric assessment had taken place without leading to a dementia diagnosis.

A quality improvement study is needed to be done to assess the effectiveness of this new pathway.

References

1. Head E, Powell D, Gold BT, Schmitt FA. Alzheimer's disease in down syndrome. Eur J Neurodegener Dis. 2012 Dec;1(3):353–364.

2. Ballard C, Mobley W, Hardy J, Williams G, Corbett A. Dementia in Down's syndrome. Lancet Neurol. 2016 May;15(6):622–636.

3. Lautarescu BA, Holland AJ, Zaman SH. The Early Presentation of Dementia in People with Down Syndrome: a Systematic Review of Longitudinal Studies. Neuropsychol Rev. 2017 Mar 13;27(1):31–45.

4. Nieuwenhuis-Mark RE. Diagnosing Alzheimer's dementia in Down syndrome: problems and possible solutions. Res Dev Disabil. 2009 Oct;30(5):827–838.

5. Määttä T, Tervo-Määttä T, Taanila A, Kaski M, Iivanainen M. Mental health, behaviour and intellectual abilities of people with Down syndrome. Downs Syndr Res Pract. 2006;11(1):37–43.

6. Sinai A, Mokrysz C, Bernal J, Bohnen I, Bonell S, Courtenay K, et al. Predictors of age of diagnosis and survival of alzheimer's disease in down syndrome. J Alzheimers Dis. 2018;61(2):717–728.

7. Eady N, Sheehan R, Rantell K, Sinai A, Bernal J, Bohnen I, et al. Impact of cholinesterase inhibitors or memantine on survival in adults with Down syndrome and dementia: clinical cohort study. Br J Psychiatry. 2018 Mar;212(3):155–160.

8. Harrison Dening K, Sampson EL, De Vries K. Advance care planning in dementia: recommendations for healthcare professionals. Palliat Care. 2019 Feb 27;12:1178224219826579.

9. Burt DB, Aylward EH. Test battery for the diagnosis of dementia in individuals with intellectual disability. Working Group for the Establishment of Criteria for the Diagnosis of Dementia in Individuals with Intellectual Disability. J Intellect Disabil Res. 2000 Apr;44 (Pt 2):175–180.

10. Evenhuis HM. The Dementia Questionnaire for People with Learning Disabilities. In: Prasher VP, editor. Neuropsychological assessments of dementia in down syndrome and intellectual disabilities. Cham: Springer International Publishing; 2018. p. 43–56.

11. Strydom A, Hassiotis A. Diagnostic instruments for dementia in older people with intellectual disability in clinical practice. Aging Ment Health. 2003 Nov;7(6):431–437.

12. Rösner P, Berger J, Tarasova D, Birkner J, Kaiser H, Diefenbacher A, et al. Assessment of dementia in a clinical sample of persons with intellectual disability. J Appl Res Intellect Disabil. 2021 Nov;34(6):1618–1629.

13. Evenhuis HM. Evaluation of a screening instrument for dementia in ageing mentally retarded persons. J Intellect Disabil Res. 1992 Aug;36 (Pt 4):337–347.

14. Walker B, MacBryer S, Jones A, Law J. Interinformant agreement of the dementia questionnaire for people with learning disabilities. Br J Learn Disabil. 2015 Sep;43(3):227–233.

15. Sheehan R, Sinai A, Bass N, Blatchford P, Bohnen I, Bonell S, et al. Dementia diagnostic criteria in Down syndrome. Int J Geriatr Psychiatry. 2015 Aug;30(8):857–863.

16. Startin CM, Hamburg S, Hithersay R, Al-Janabi T, Mok KY, Hardy J, et al. Cognitive markers of preclinical and prodromal Alzheimer's disease in Down syndrome. Alzheimers Dement. 2019 Feb;15(2):245–257.

17. Evenhuis HM. Further evaluation of the Dementia Questionnaire for Persons with Mental Retardation (DMR). J Intellect Disabil Res. 1996 Aug;40 (Pt 4):369–373.

18. Prasher VP. Dementia Questionnaire for Persons with Mental Retardation (DMR): Modified Criteria for Adults with Down's Syndrome. J Appl Res Int Dis. 1997 Mar;10(1):54–60.

19. Ball SL, Holland AJ, Treppner P, Watson PC, Huppert FA. Executive dysfunction and its association with personality and behaviour changes in the development of Alzheimer's disease in adults with Down syndrome and mild to moderate learning disabilities. Br J Clin Psychol. 2008 Mar;47(Pt 1):1–29.

20. Torr J. Assessment of dementia in people with learning disabilities. Adv Mental Hlth Learn Disabil. 2009 Sep 23;3(3):3–9.

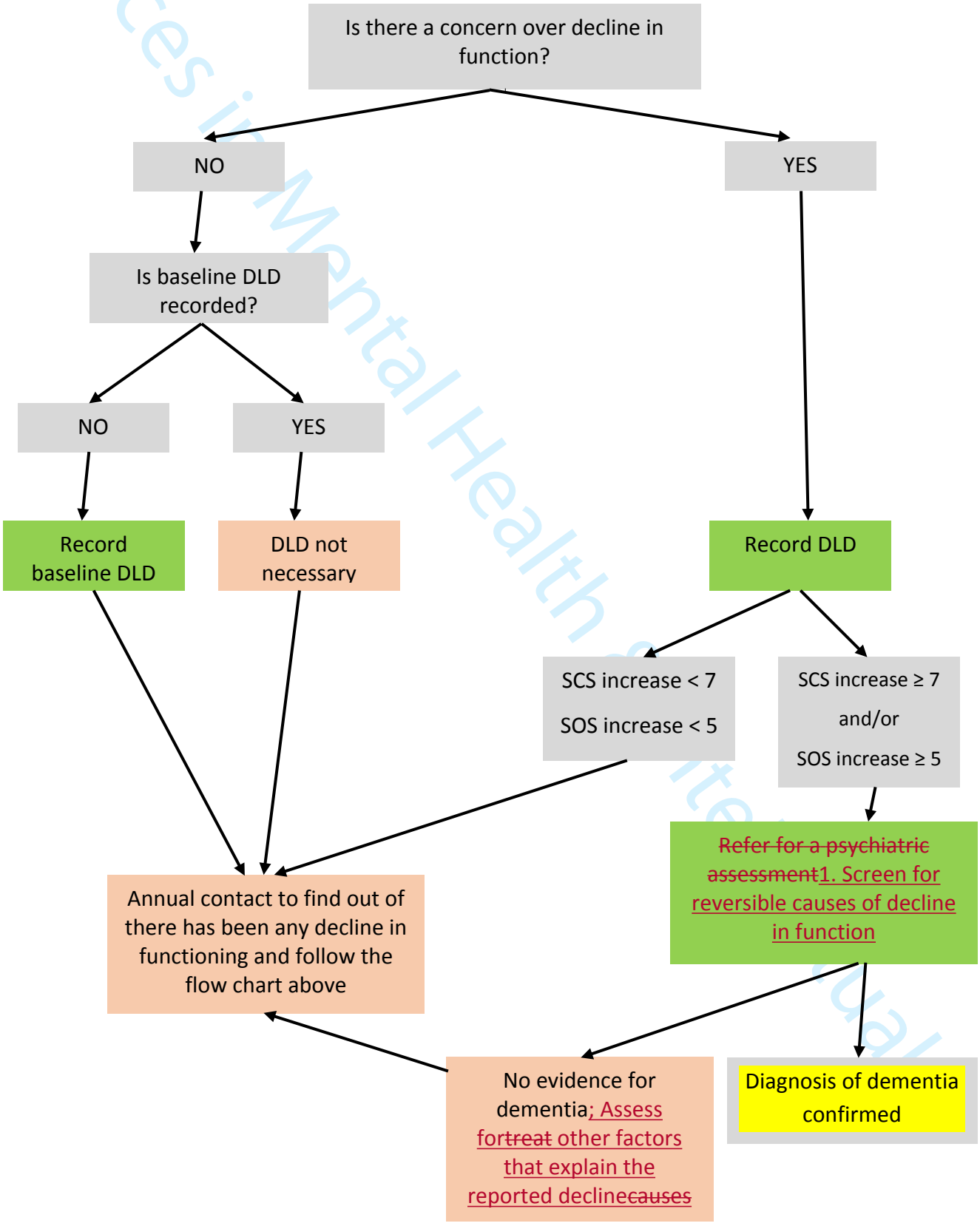
21. McBrien J. Screening Adults with Down's Syndrome for Early Signs of Dementia. Journal of Integrated Care. 2009 Jun 26;17(3):3–7.

22. Stanton LR, Coetzee RH. Down's syndrome and dementia. Advances in Psychiatric Treatment. 2004 Jan;10(1):50–58.

Appendix 1: Decision tool

DLD in adults with Down's Syndrome: decision tool

This tool is designed to advise if performing a DLD is necessary for this patient.



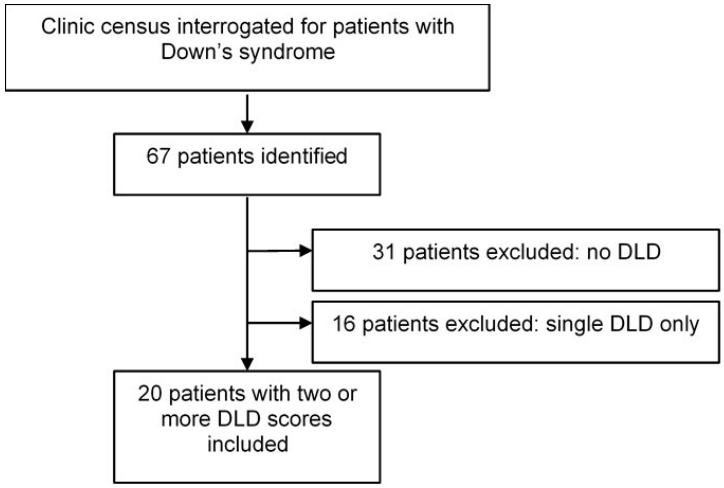


Figure 1. Flow-chart outlining patient recruitment process

160x80mm (150 x 150 DPI)

	SCS increase of ≥ 7 points between assessments	No SCS increase of ≥ 7 points between assessments
Confirmed diagnosis of dementia (5)	4	1
No diagnosis of dementia (15)	6	9

Table 1: Sensitivity and specificity two-by-two tables for DLD Cognitive scores in diagnosis of dementia. N=20.

159x73mm (600 x 600 DPI)

	SOS increase of ≥ 5 points between assessments	No SOS increase of ≥ 5 points between assessments
Confirmed diagnosis of dementia (5)	1	4
No diagnosis of dementia (15)	4	11

Table 2: Sensitivity and specificity two-by-two tables for DLD Social scores in diagnosis of dementia. N=20.

159x73mm (600 x 600 DPI)

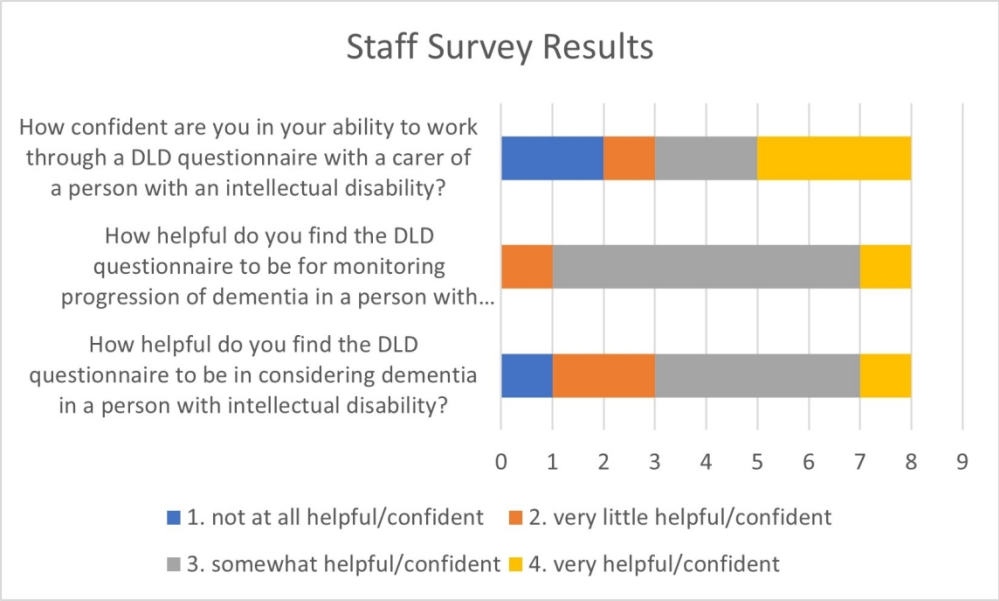


Figure 2. Results from staff survey (n=8) asking the following 3 questions: 1. How confident are you in your ability to work through a DLD questionnaire with a carer of a person with an intellectual disability? 2. How helpful do you find the DLD questionnaire to be for monitoring progression of dementia in a person with intellectual disability? 3. How helpful do you find the DLD questionnaire to be in considering dementia in a person with intellectual disability?

127x76mm (330 x 330 DPI)

Appendix 1: Decision tool

DLD in adults with Down's Syndrome: decision tool

This tool is designed to advise if performing a DLD is necessary for this patient.